TFW 1634

TRANSMITTAL LETTER (General - Patent Pending)	Docket No. UMD-0097

In Re Application Of: **Mandola et al.**

Application No.	Filing Date	Examiner	Customer No.	Group Art Unit	Confirmation No.
10/532,201	June 27, 2005	Not yet assigned	46046	1634	2039

Title: **Thymidylate Synthase Polymorphisms for Use in Screening for Cancer Susceptibility**

COMMISSIONER FOR PATENTS:

Transmitted herewith is:

Courtesy Copy of International Preliminary Examination Report

in the above identified application.

- ☒ No additional fee is required.
- ☐ A check in the amount of is attached.
- ☒ The Director is hereby authorized to charge and credit Deposit Account No. **50-1619** as described below.
  - ☐ Charge the amount of
  - ☒ Credit any overpayment.
  - ☒ Charge any additional fee required.
- ☐ Payment by credit card. Form PTO-2038 is attached.

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

Jane Massey Licata

Signature

Dated: **December 9, 2005**

Jane Massey Licata, Reg. No. 32,257

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to the "Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" [37 CFR 1.8(a)] on

December 9, 2005
(Date)

Mariana Lennox

Signature of Person Mailing Correspondence

Mariana Lennox

Typed or Printed Name of Person Mailing Correspondence

cc:

PATENT COOPERATION TREATY

OCT 20 2005

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:
MICHAEL J. WISE
PERKINS COIE LLP
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SEATTLE, WA 98111-1209

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PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Applicant's or agent's file reference 547048060WO UMD-0054	Date of Mailing (*day/month/year*) 14 OCT 2005
	IMPORTANT NOTIFICATION

International application No.	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/US03/33441	21 October 2003 (21.10.2003)	21 October 2002 (21.10.2002)

Applicant

UNIVERSITY OF MEDICINE AND DENTISTRY OF NEW JERSEY

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/ US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Juliet Switzer Telephone No. 571 272 1600

Form PCT/IPEA/416 (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 547048060WO	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US03/33441	International filing date *(day/month/year)* 21 October 2003 (21.10.2003)	Priority date *(day/month/year)* 21 October 2002 (21.10.2002)
International Patent Classification (IPC) or national classification and IPC IPC(7): C07H 21/04; C12Q 1/70 and US Cl.: 435/6, 91.2; 536/23.1		
Applicant UNIVERSITY OF MEDICINE AND DENTISTRY OF NEW JERSEY		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of report with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
21 May 2004 (21.05.2004)	15 September 2005 (15.09.2005)
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/ US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Juliet Switzer Telephone No. 571 272 1600

Form PCT/IPEA/409 (cover sheet)(July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US03/33441

I. Basis of the report

1. With regard to the elements of the international application:*

☒ the international application as originally filed.

☒ the description:
pages 1-70 as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the claims:
pages 70-73, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the drawings:
pages 1-12, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the sequence listing part of the description:
pages 1-3, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☒ contained in the international application in printed form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages NONE

☐ the claims, Nos. NONE

☐ the drawings, sheets/~~fig~~ NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

*** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US03/33441

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

- ☐ restricted the claims.
- ☒ paid additional fees.
- ☐ paid additional fees under protest.
- ☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention is accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.
- ☒ not complied with for the following reasons:

Group 1, claims 1-10, drawn to isolated nucleic acid molecules, probes and kits.

Group 2, claims 11-20, drawn to methods for determining whether an individual has a heightened predisposition to cancer or cardiovascular disease.

There is no special technical feature which joins groups I and II, as the methods of claim 11 do not recite or require the products of claim 1 or invention 1. Even if they were to recite or require the products of the main invention, the main invention does not represent an advance in view of the prior art. Lou et al. (GenBank AF279906) teach an isolated nucleic acid comprising SEQ ID NO: 1, wherein G is replaced by C at nucleotide 12 (see nucleotides 132-159 of Lou et al.). Furthermore, with regard to claim 3, Dean et al. (US6087489) teach a single-stranded nucleic acid probe that hybridizes to the isolated nucleic acid molecule of claim 1. Specifically, SEQ ID NO: 16 taught by Dean et al. is a 20mer nucleic acid probe which is complementary to nucleotides 7-26 of instant SEQ ID NO: 1, wherein G is replaced by C at nucleotide 12. PCT Rule 13.2 states "The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art (emphasis added)." Since the main invention was known at the time of filing, there is a lack of unity of invention between group 1 and group 2.

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☒ all parts.
- ☐ the parts relating to claims Nos. ____

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US03/33441

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims 11-20	YES
	Claims 1-10	NO
Inventive Step (IS)	Claims 11-20	YES
	Claims 1-10	NO
Industrial Applicability (IA)	Claims 1-20	YES
	Claims NONE	NO

2. CITATIONS AND EXPLANATIONS
Please See Continuation Sheet

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

V. 2. Citations and Explanations:

Claims 1-2 lack novelty under PCT Article 33(2) as being anticipated by Database NCBI Accession Number AF279906.

The record teaches an isolated nucleic acid molecule of SEQ ID NO: 1 wherein G is replaced by C. Nucleotides 132-159 of the sequence taught in the record are identical to instant SEQ ID NO: 1 nucleotides 1-28 wherein the G is replaced by a C. With regard to claim 2, the nucleic acid taught by the record also comprises a nucleic acid "of" SEQ ID NO: 1, since the language "of" is broadly interpreted to mean that the claimed nucleic acid must only contain a fragment of SEQ ID NO: 1, which the nucleic acid taught by the accession record does teach.

Claims 3-10 lack an inventive step under PCT Article 33(3) as being obvious over Database NCBI Accession Number AF279906.

The record teaches an isolated nucleic acid molecule of SEQ ID NO: 1 wherein G is replaced by C. Nucleotides 132-159 of the sequence taught in the record are identical to instant SEQ ID NO: 1 nucleotides 1-28 wherein the G is replaced by a C. The nucleic acid taught in the record is genomic DNA.

The record does not teach a single stranded probe as required in claim 3, nor a detectable label on the probe as required by claim 5, nor the additional elements of a kit as required by claim 6-8. With regard to claims 9-10, these are statements of intended use but do not appear to structurally modify the claimed invention.

The differences between the claims and the reference, however, do not involve inventive step because at the time the invention was made, it was routine within the technology to make a single stranded probe of one strand of a double stranded DNA in order to provide a probe for the detection of a molecule of interested. In this case, the record teaches that this nucleic acid represents a novel allele for the thymidylate synthase gene, and thus, one would have been motivated to provide a single stranded probe for detection of the allele. Furthermore, it would have been obvious to put the probe into a kit in order to provide practitioners with a simple method for obtaining the probe. It is also noted that it would have been obvious to have made additional probes and primers that were portions of the sequence provided within the record in order to have provided molecules for the amplification of the novel allele. These primers would have routinely been within the range of 17-35 nucleotides.

Therefore, the claimed invention lacks an inventive step in view of the disclosure of the thymidylate synthase sequence provided by the record.

Claims 1-10 lack novelty under PCT Article 33(2) as being anticipated by Dean et al. (US6087489).

Dean et al. teach a single stranded nucleic acid molecule that is identical to the complement of nucleotides 7-26 of SEQ ID NO: 1, wherein nucleotide 12 is replaced with a C, see SEQ ID NO: 16 of the patent. This is considered to meet the limitations of claims 1 and ~~2 because this nucleotide a sequence "of SEQ ID NO: 1" as this term is interpreted broadly to require only that a fragment SEQ ID NO: 1~~